201-15171

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ASSOCIATES INC.

April 9, 2004

Oscar Hernandez
HPV Chemicals Branch
Risk Assessment Division
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue
Washington, DC 20460

Dear Dr. Hernandez:

The LAB Sulfonic Acids Coalition (Coalition) consists of five member companies (Colgate-Palmolive Company, Akzo Nobel Surface Chemistry LLC, The Dial Corporation, Stepan Company, and Unilever HPC-USA) and is independent of any other HPV Challenge Program or OECD SIDS Consortium. The Coalition is submitting a revised and final assessment plan report and robust summary document for the Linear Alkylbenzene (LAB) Sulfonic Acids category. These revised documents address all comments provided by the United States Environmental Protection Agency (EPA). The revised documents also address a guinea pig sensitization study (recent TSCA 8e submission) on a mixture of materials that included 17.5% dodecylbenzene sulfonic acid (CAS No. 27276-87-0).

An overview of the revisions is presented herein to facilitate further review by EPA and other interested parties. Overall, the EPA comments can be classified into two general groups.

1) Requests for additional detail to be added into the robust summaries
2) Clarification of the relationship between LAB sulfonic acids and supporting or surrogate substances
3) Clarification of the adequacy of the ecological data and request for additional detail

Each of these areas is discussed in more detail below. Pertinent modifications have been made to the assessment plan and robust summary documents. Detailed responses to specific EPA comments are included as an appendix to this letter.

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Founding Partner, The WORLDCOM Group, Inc. with over 100 offices worldwide.

The Coalition agrees with EPA's statement that the data and rationale adequately support the justification of the LAB Sulfonic Acids category. Furthermore, EPA states that adequate data are available to characterize the physicochemical properties, environmental fate, and health effects of the category. The Coalition is in agreement with EPA that the data are sufficient for the purposes of the HPV Challenge Program and is confident that the additional data elements added to the robust summaries for the ecological endpoints will be also be adequate.

Provision of Additional Detail in the Robust Summaries

EPA agreed that the available data adequately characterized the physical-chemical properties, environmental fate, and mammalian toxicity of the category. However, EPA also indicated that additional detail should be added to some of the robust summaries to improve the clarity and interpretation of the study quality. Therefore, the Coalition has again reviewed each of the robust summaries and acquired additional primary literature when it was available. Any additional detail that could be derived from the data sources was added to the robust summaries. Additional information was also added to the assessment plan report where needed to assist in the evaluation of the available data.

Overall, the available data are consistent, indicate that the chemicals are highly susceptible to photodegradation and biodegradation, and show a lack of significant toxicity.

Clarification of the relationship between LAB sulfonic acids and the supporting or surrogate substances

Several EPA comments suggested that the relationship between LAB sulfonic acids and its supporting substances needed to be clarified. This relationship is discussed in the assessment report under the section heading "Identification of Structure Based Category." As indicated in Table 2 of the assessment report, three LAB sulfonic acids are being sponsored in this category (CAS Nos. 68584-22-5, 27176-87-0, 25496-01-9). Although not sponsored by this Coalition, European LAB sulfonic acids, CAS # 85536-14-7, are included as a supporting substance, as noted in Table 2, because the alkyl chain distribution closely matches that of one of the sponsored sulfonic acids, CAS # 68584-22-5. LAS, also not sponsored by the Coalition, is included in Table 2 as a supporting substance because of the close chemical relationship of the LAB sulfonic acids to LAS in aqueous solutions at neutral (physiological) pH values. All data for LAS were taken from the LAS hazard assessment already compiled and submitted under the OECD SIDS program. The ten CAS numbers identified for LAS in Table 2 of the LAB sulfonic acid assessment report are all considered to be the single entity encompassed by the chemical name LAS and therefore need not be discussed individually. Data for a related surrogate substance were included only where appropriate to understand the fate or toxicity of the LAB sulfonic acids.

As described in depth in the assessment report, LAB sulfonic acids are intermediates in the manufacture of LAS surfactants. A figure in the assessment report shows the structures of LAB, LAB sulfonic acids, and LAS and the manufacturing processes by which they are related. EPA has stated in its comments that the category is adequately justified and all comparisons with LAS as the supporting substance are appropriate.

Clarification of the adequacy of the ecological data and request for additional detail

EPA states that adequate data are available to characterize the physicochemical properties, environmental fate, and health effects of the category. However, in its comments EPA indicates that it is reserving judgment on the adequacy of the ecological endpoints pending receipt of certain data elements in the robust summaries.

The Coalition is confident that there are sufficient data available to adequately characterize the ecological endpoints for the LAB sulfonic acids. To address EPA's comments, the Coalition has re-evaluated all of the original study reports and literature and added significant additional details to the robust summaries when available. Specifically, data have been added on the water quality characteristics (pH, hardness, temperature, dissolved oxygen), test substance purity, number of organisms per group, number of replicates, actual test concentrations, use of appropriate controls, signs of toxicity, statistical methods, and other study details as available. Additional information was also added to the assessment plan report where needed to assist in the evaluation of the available data. These additional data confirm study reliability and provide confidence in the overall evaluation of the results.

Summary

The LAB Sulfonic Acids Coalition has provided a revised assessment plan report and robust summaries for the LAB Sulfonic Acids category. The Coalition has made every attempt to address the comments received from EPA in these revised documents.

The Coalition has provided additional detail in the robust summaries to assist in the evaluation and interpretation of study quality. The relationship between LAB sulfonic acids and the supporting substances has been further clarified. The data supporting the ecological endpoints was further reviewed and additional details were added to the robust summaries and assessment plan as available and appropriate.

The Coalition is in agreement with the USEPA that the LAB sulfonic acids are a valid category for purposes of the HPV Challenge Program. The Coalition is also in agreement with the USEPA that the available data adequately characterize the physicochemical properties, environmental fate, and health effects of the category. Furthermore, the Coalition is confident that the same conclusion is appropriate for the ecological endpoints and additional information has been added to support this conclusion. LAB sulfonic acids are

used exclusively as intermediates in the production of LAS. Worker exposure is extremely limited and highly controlled through engineering controls, personal protective equipment, and the use of closed production systems. There is no consumer exposure to LAB sulfonic acids since they are not used in consumer products.

If you have any questions regarding the final assessment plan report or the robust summaries, please contact me at 202-737-8400 (telephone), 202-737-8406 (fax) or jheinze@johnadams.com (email).

Sincerely,

John E. Heinze, Ph.D.
Senior Vice President, Science
John Adams Associates Inc.

cc: David J. Kent, Compliance Services International

Appendix
Specific Responses to EPA Comments on the
Linear Alkylbenzene (LAB) Sulfonic Acids Category

SUMMARY OF EPA COMMENTS

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The data and rationale provided adequately support the category.

The Coalition is in agreement with EPA comments.

2. Physicochemical Properties and Environmental Fate. The submitter needs to provide vapor pressure data for at least two of the category members and state the input values used in fugacity models in the robust summaries.

Estimated vapor pressure data and information regarding the fugacity model inputs have been added to the documents.

3. Health Effects. Adequate data are available for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

The Coalition agrees with EPA comments that adequate data are available. Additional study details have been added to the robust summaries.

4. Ecological Effects. EPA reserves judgment on the adequacy of all ecological endpoints pending receipt of critical missing data elements in the robust summaries.

Additional study details have been added to the robust summaries and the Coalition is confident that adequate data are now available for the ecological endpoints.

DETAILED EPA COMMENTS ON THE LINEAR ALKYLBENZENE (LAB) SULFONIC ACIDS CATEGORY CHALLENGE SUBMISSION

General

The test plan did not discuss all of the substances for which robust summaries were submitted–for example, a C_{10}-C_{14} derivative (CAS No. 69669-44-9) that was the subject of the submitted repeated-dose oral toxicity assay.

All of the substances included in the robust summaries were discussed in the assessment plan as appropriate. The C10-14 derivative (CAS No. 69669-44-9) is one representative of LAS. This was clarified in the assessment plan and the additional CAS numbers added to Table 2.

Category Definition

The submitter proposed the linear alkylbenzene (LAB) sulfonic acids category to cover three sponsored substances containing para-*sec*-alkyl-substituted benzenesulfonic acids and eight non-sponsored substances to provide supporting data:

Four of the supporting substances, CAS Nos. 1322-98-1, 26248-24-8, 27636-75-5, and 68081-81-2, were listed in Table 2 of the test plan but could not be identified in the robust summaries; i.e., no data were provided on these substances. The submitter needs to reconcile the apparent discrepancy. CAS No. 85536-14-7 is referred to as European LAB sulfonic acids in the test plan and robust summaries and was added as a representative substance to fill data gaps for the sponsored substance, CAS No. 68584-22-5. The remaining seven non-sponsored substances are produced from LAB sulfonic acids by neutralization to produce the associated sodium salts.

Finally, several other linear alkylbenzene sulfonates are included in the robust summaries only to provide additional supporting data but are not listed in Table 2 of the test plan. These substances are: $C_{10\text{-}14}$ benzene sulfonic acid, sodium salt (CAS No. 69669-44-9); alkylbenzene sulfonate, sodium salt (commercial name P-500 N-Na, no CAS No. given); and linear $C_{10\text{-}13}$-alkylbenzene sulfonic acid (commercial name dobanic acid, no CAS No. given). The submitter needs to list these substances in Table 2 in the test plan as well.

Table 2 is intended to list the substances being sponsored. The Coalition is sponsoring only the three LAB sulfonic acid substances. LAS is included as a supporting substance because both LAS and the LAB sulfonic acids will exist in the dissociated state at environmental and physiological pH levels. It is important to note that the term LAS encompasses several different CAS numbers, as reported in a separate submission by the Industry Coalition for the SIDS Assessment of LAS (Industry Coalition). All CAS numbers encompassed by LAS have

therefore been included in Table 2, however, data are not necessarily available for each CAS number; the sum total of all CAS numbers are representative of LAS. In addition, there are some cases where the study reports the test substance only as LAS or Japan LAS. While specific CAS numbers are not provided, they likely would be one of the CAS numbers listed. For the purposes of the LAB sulfonic acid category, the Coalition relied on the most representative data for each endpoint, as determined by the Industry Coalition.

Category Justification

The submitter supports the LAB sulfonic acid category on the basis of the structural similarity and narrow range of alkyl chain length that will result in similar physicochemical, environmental fate, and toxicological properties of the category members. As noted above, the submitter used the sodium salts of alkylbenzene sulfonic acids (LAS) as representative of the category members because both LABs and LASs will exist in the dissociated state at environmental and physiological pHs. The submitter also noted that LAB sulfonic acids and LASs will differ for some physicochemical properties, such as melting point, boiling point, and vapor pressure, because LASs are salts, and these "are not appropriate to compare." The submitter's approach and use of LAS as representative of LAB sulfonic acids for certain endpoints are reasonable.

The LABs have low melting points and high measured water solubilities, and the single measured log K_{ow} value in the category of 2 for $C_{10\text{-}16}$-alkyl derivatives of benzene sulfonic acid is similar to the calculated values of 1.96 and 2.52 for CAS Nos. 25155-30-0 and 26248-24-8, respectively. Although there are some inconsistencies in the values (e.g., boiling points), other physicochemical data help support the category.

Given their similar structures, the three sponsored substances are expected to have similar fate properties. Biodegradation data are available for CAS Nos. 85536-14-7, 27176-87-0 and 68411-30-3. These data are consistent and consequently support the category.

Limited comparative health effects data were provided to support the category. Acute oral LD_{50} values were in the same range for CAS Nos. 68584-22-5 and 27176-87-0 and two analogs, CAS Nos. 68411-30-3 and 85536-14-7. CAS No. 27276-87-0 was found to be corrosive and the analog CAS No. 85536-14-7 was found to be highly irritating in skin irritation tests in guinea pigs. Bacterial mutagenicity testing was negative for CAS No. 68584-22-5 and the analog, CAS No. 68411-30-3. Similarities in other health effects are to be expected because of the narrow range of alkyl chain lengths of category members.

Although EPA is reserving judgment on the adequacy of submitted ecological data, similarities in ecological effects are expected because of the narrow range of alkyl chain lengths of category members.

Overall, the data and reasoning provided adequately support the category.

The Coalition agrees with EPA that the category is adequately justified and that the use of LAS as representative of LAB sulfonic acids for certain endpoints is reasonable. We agree that sufficient data are available for physicochemical properties, environmental fate, and health effects to support the category. While EPA indicates in its comments that it reserves judgment on the adequacy of the submitted ecological data, the Coalition agrees with EPA that similarities in ecological effects expected due to the structural similarity and function of the LAB sulfonic acids. More details have been added to the robust summaries to further assist EPA in reaching acceptance of the adequacy of the ecological data.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility)

The data provided by the submitter for melting point, boiling point, octanol/water partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program.

The Coalition agrees with EPA.

Table A-1 does not indicate which data are measured and which are estimated. The table also does not always indicate when a surrogate material is used to satisfy the endpoint.

Table A-1 summarizes the data values for each endpoint. Further information on the data is described as appropriate in the assessment plan and all details for each study or modeled result are explained in the robust summaries.

Melting point. **The category members are mixtures and will not have well-defined melting points. The submitter provided several melting points in the range < -10 °C to 10 °C. No further testing is necessary.**

The Coalition agrees with EPA.

Boiling point. **The submitter provided boiling points of 315 and 205 °C for dodecylbenzenesulfonic acid. The submitter also provided a boiling point of 156 °C for a C10-C12 mixture. EPA estimations (MPBPWIN v1.41) for representative structures were 430, 453, and 465, respectively. While there is no clear agreement between the boiling points provided by the submitter and those found in the literature or by**

estimation, the category members are mixtures and will not have well defined boiling points. The estimated boiling points further suggest that the boiling points of category members would be >300 °C and that testing is thus not needed for this endpoint.

The Coalition agrees that the data are sufficient for the HPV Challenge Program and no further testing is warranted.

Vapor pressure. **The submitter did not provide vapor pressure data for any of the category members. The submitter provided a vapor pressure of 0.22 hPa (0.17 mm Hg) (no temperature stated) for an alkylbenzene sulfonic acid that contained 18.3% of n-decylbenzenesulfonic acid (CAS No. 140-60-3), 42.1% of Undecylbenzenesulfonic acid (CAS No. 50854-94-9), and 30.0% of dodecylbenzenesulfonic acid (CAS No. 27176-87-0). The vapor pressure for this substance is questionable. If determined at 25 °C, the value is much higher than the estimated vapor pressures of the three main components, which range from 10^{-9} to 10^{-11} mm Hg at 25 °C. Therefore, the data provided by the submitter are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide vapor pressure data following OECD guidelines for at least two members of this category in order to have an accurate assessment of this endpoint. According to OECD guidelines, estimated values below 10^{-5} Pa (10^{-8} mm Hg) are acceptable.**

To better characterize the vapor pressure of the LAB sulfonic acids, the Coalition conducted additional estimates using the EPA EPI Suite software. Results indicated that all three LAB sulfonic acids have very low vapor pressures (i.e., all below 10^{-8} Pa). As indicated by EPA, these data are acceptable for the purposes of the HPV Challenge program and have been added to the robust summary document and described in the assessment report.

Partition coefficient. **The category members are surfactants and measurement of a log K_{ow} will be problematic. EPA agrees with the submitter that the LAB acids and their sodium salts will be completely ionized (pK_a <1) in solution at environmentally relevant pHs and comparisons between the two will be appropriate. The log K_{ow} values for sodium dodecylbenzenesulfonate (CAS No. 25155-30-0) and sodium dodecylbenzenesulfonate (CAS No. 25155-30-0) reasonably represent the category members.**

The Coalition agrees with EPA.

Water solubility. **The category members are surfactants and measurement of water solubility is problematic. Since they form micelles in water, they may be better described as dispersible rather than miscible in water. As with log K_{ow}, comparison of the sodium salts and the acids is appropriate. Although estimated values might provide reasonable theoretical water solubilities for these chemicals, EPA suggests that the**

submitter consider whether it is more appropriate to cite available data on critical micelle concentrations of the salts.

The Coalition has considerable experience with surfactant materials and agrees that the evaluation of water solubility is problematic. To assist in the characterization, the critical micelle concentration (CMC) of LAS has been added to the robust summary document and summary table. The discussion of water solubility in the assessment plan has also been expanded.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation, stability in water, biodegradation, and transport and distribution (fugacity) are adequate for the purposes of the HPV Challenge Program.

Fugacity. **The submitter needs to provide the input values used in fugacity models in the robust summaries.**

The Coalition agrees that the environmental fate data are adequate for the HPV Challenge Program. In addition, the EPA EPI Suite software was used to estimate the fugacity for the LAB sulfonic acids. EPI Suite utilizes input values for relevant physicochemical parameters from its resident database, which has undergone extensive peer review and is accessed by input of the CAS number. This information has been indicated in the robust summaries.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for the acute toxicity endpoint for two category members (CAS Nos. 68584-22-5 and 27176-87-0) and for gene mutations for CAS No. 68411-30-3, an analog, for the purposes of the HPV Challenge Program. The data for chromosomal aberration for CAS No. 85536-14-7, a European LAB sulfonic acid, are acceptable, but the robust summary needs revision. The data submitted for the repeated-dose, reproductive and developmental toxicity endpoints for analogs, CAS No. 69669-44-9, LAS C10-C14, sodium salt (no CAS No. given), and a Japan LAS (average alkyl chain length = C11.7-12.3; no CAS No. given), were summarized from a secondary source and reviewed by the International Program on Chemical Safety (IPCS), and were accepted by the OECD SIDS Program. Therefore, these data are acceptable for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

The Coalition agrees that adequate data are available for the acute toxicity, gene mutation, repeated dose, reproductive, and developmental toxicity endpoints. As requested, additional information has been added to the robust summaries on chromosome aberration.

Genetic toxicity. **The test plan (p. 14) indicated that *in vivo* genotoxicity data were provided for CAS No. 68584-22-5; however, the submitted data were for CAS Nos. 85536-14-7 and 69669-44-9. The submitter needs to address this discrepancy.**

The test plan has been modified to clarify where data for surrogate substances were used to support the LAB sulfonic acid category.

Ecological Effects (fish, invertebrates, and algae)

EPA reserves judgment on the adequacy of the fish, daphnia, and algae studies pending receipt of critical missing data elements in the robust summaries (*see* Specific Comments on the Robust Summaries below).

The Coalition is confident that the available aquatic ecological effects data are adequate to characterize the effects of LAB sulfonic acids on these taxa. To assist EPA in making this determination, all of the studies related to ecological effects have been re-evaluated. Considerable additional details on the conduct of each study have been added to the robust summaries.

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. **A robust summary for an acute oral toxicity study on CAS No. 68584-22-5 in rats is missing the purity (or activity as stated in the robust summaries) of the test substance and a range or 95% confidence interval for the LD50. The submitter needs to clarify whether a group of three fasted females was also treated with the starting 2000 mg/kg/bw dose.**

Additional information to clarify that three fasted females were treated at 2000 mg/kg bw has been added to the robust summary (page 32/56).. The activity of the LAS tested was not reported.

Genetic toxicity. **Missing information in a robust summary for a reverse mutation assay in *Salmonella typhimurium* for the supporting compound, CAS No. 68411-30-3, includes the concentration levels (only a range was given), the number of replicates per concentration, the positive and negative controls, the source of the metabolic activation**

system, the number of colonies per concentration that were counted, and the criteria for positive results.

Additional information on the concentrations tested, number of replicates, S9 metabolic activation, and negative and positive controls has been added to the robust summary (page 43/56).

Although an *in vivo* micronucleus assay in mice treated with an analog, CAS No. 85536-14-7, was an OECD guideline study, the robust summary is missing critical information including the gavage vehicle, the number of animals tested, the concentration levels, the positive and negative controls, the time of exposure, the number of erythrocytes examined, the criteria for positive results, and the data for exposures less than 72 hours (if available).

Additional information on the test substance purity, number of animals tested, concentration level, and negative and positive controls has been added to the robust summary (page 44/56).

Reproductive toxicity. **A robust summary for a 3-generation reproductive toxicity assay in rats exposed to C_{10}-C_{14} LAS, sodium salt analog, in diet, was missing the CAS registry number for the test substance and details about the specific parameters that were evaluated.**

A specific CAS number was not reported as the study was conducted on a commercial LAS material. The standard reproductive toxicity study parameters were evaluated and no effects were observed, as listed in the results of the robust summary (pages 46-7/56).

Developmental toxicity. **A robust summary for a developmental toxicity assay in rats exposed to Japan LAS was missing the CAS registry number, cation, and the purity of the test substance and details about the specific parameters that were evaluated (both maternal and fetal).**

A specific CAS number for LAS was not provided. The study represents the most NOAEL value as determined by the Industry Coalition for the SIDS Assessment of LAS after reviewing 10 developmental studies conducted on LAS (page 47/56).

<u>Ecological Effects</u>

Study details were missing in all of the submitted summaries.

Fish. **Missing study details included the following: test substance purity, number of fish per group, age and mean weight of the fish, test concentrations, use of appropriate controls, signs of toxicity, water quality characteristics (*e.g.*, hardness, pH, dissolved**

oxygen, alkalinity, and temperature), control response, statistical methods, and 95% confidence limits.

Invertebrates. **Missing study details included the following: test substance purity, age and number of daphnia per group, test concentrations, use of appropriate controls, signs of toxicity, water quality characteristics (*e.g.*, hardness, pH, dissolved oxygen, alkalinity, and temperature), control response, statistical methods, and 95% confidence limits.**

OECD 202 ("Acute Immobilization Test in Daphnia sp.") recommends that the pH of the controls and test solutions be measured at the beginning and the end of the test, and that the pH of the test solutions not be adjusted. It was not clear from the inadequate details in the summaries that these recommendations were followed.

Algae. **Missing study details included the following: test substance purity, test concentrations, number of replicates per group, culturing apparatus, culture conditions (*e.g.*, lighting and temperature), use of appropriate controls, control response, statistical methods, and 95% confidence limits.**

The Coalition re-evaluated all of the aquatic toxicity studies and has added a considerable amount of details on study conduct to each of the relevant robust summaries (pages 21-9/56). The Coalition is confident that the ecological effects of the LAB sulfonic acids are adequately characterized for the purposes of the HPV Challenge Program.